PLT Docket 97N-0289

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

May 10, 1999

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Rosario Zisa, C.P.A.
373 North 1th Street
Prospect Park, New Jersey 07508-2234

Dear Mr. Zisa,

Thank you for your April 22, 1999, letter to Dr. Woodcock in which you expressed your concern with changing language for pregnancy labeling. She referred your letter to me for response. As you are aware, the FDA is currently reevaluating the pregnancy labeling categories. The overwhelming message FDA received from the speakers at the Part 15 Hearing held in October 1997 indicated that pregnancy categories should be eliminated and replaced with something more informative.

The FDA has an established Pregnancy Labeling Task Force that has been working on this topic to determine the best course of action. They have reviewed the comments received in the public docket, have completed preliminary focus testing of current labeling, and are developing draft guidance.

I am sending a copy of your letter to the official docket and the chair of the Task Force. Your recommendations will become part of the public record and will be considered as FDA makes its decision regarding any necessary pregnancy labeling changes.

Once again, thank you for your observations and recommendations.

Sincerely,

Rose E. Cunningham
Project Manager, Pregnancy Labeling Task Force
Center for Drug Evaluation and Research

97N-0289

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April 22, 1999

Janet Woodcock, MD, Director
Center for Drug Evaluation and Research
Federal Drug Administration
56 Fishers Lane
Rockville, MD, 20857

Re: The FDA for Drugs Use-in-Pregnancy [Title 21 CFR 201.57]. . . ought to continue to maintain **Schedule D** with an unequivocal and strong proviso. . . ***". . . if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective."***

Dear Dr. Woodcock:

It is my understanding that currently the FDA is reevaluating the Labeling for Human Prescription Drugs–Pregnancy Labeling Categories. If I may and, with the utmost respect, I would like to bring to your attention that for Drugs for Use-in-Pregnancy, and in particular for **Category D** [which includes ***barbiturates,*** i.e., Secobarbital (Seconal)] the description ***ought to be maintained*** with the current unequivocal and strong proviso: i.e., ***to treat serious disease in pregnant women,*** and specifically ***". . . if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective."*** This, I believe is in accordance to Title 21 CRF 201.57 [or, Federal Register Volume 44, No. 124, at page 37464, dated Tuesday, June 26, 1979, Rules and Regulations,] which I respectfully would like to paraphrase for your convenience:

> "**Pregnancy category D.** If there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks (***for example, if the drug is needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective). . . .***"

I have noted that drugs and medical reference *icons* in the Healthcare Industry, i.e., the United States Pharmacopeia Dispensing Information (USP DI) [at page 492–Barbiturates/Pregnancy,] Physicians' Desk Reference (PDR), Mosby's GenRx the Complete Reference of Generic and Brand Drugs, the Merck Manual of Diagnosis and Therapy, Springhouse's Physician Drug Handbook, S.W. Saunders' Nursing Drug Handbook, Appleton & Lange's Health Professional Drug Guide (all the editions referenced are for 1999, with the exception of USP DI which refers to the one of 1998) etc., share a similar terminology that is purely unequivocal, strong, and clear to the point to stress a very serious concern, that's , that Schedule D drugs in Pregnancy would only prescribed, as per Title 21 CFR 201.57, ". . . *if the drug is needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective. . . .*" Similarly, it is my understanding that Category D's Drugs Use-in-Pregnancy, (barbiturates and Secobarbital being one of them,) would be prescribed ***only*** and ***if*** **to treat 'serious' diseases in pregnant women** . . . because *one* of the dreadful risks of barbiturates, in the context of prenatal obstetrical analgesia, is '***respiratory***' and '***vasomotor***' ***depression***. Please consider a

scenario where a "***verbal/oral prescription***" of ***200 milligrams of Secobarbital/Seconal*** was prescribed in the *middle of the night*, when there were ***no emergencies*** . . . where the patient experienced labor pains consistent to millions and millions of women who are going to give birth . . . where the *membrane was broken* and *part (was) not palpable* . . . [and considering that the patient's weight was not an issue, 200 milligrams of Secobarbital/Seconal--a *preoperative dosage* which requires that a surgery is performed in 1 or 2 hours] then the obstetrician did not follow up for a total of eleven (11) hours. In short, the foregoing *is* in direct contrast to the directives of DEA's Title 21 USC Section 829--Prescriptions, whose heart of the matter is: " . . . ***In case of emergency, oral prescriptions for schedule II substances may be filled . . .***"

I understand that Title 21 CFR 201.57 principally addresses the '*teratogenic*' issue for Drugs's Use-in-Pregnancy, and am I also aware that Title 21 USC 829--Prescriptions, for Schedule II addresses the '*high potential for abuse, physical and psychological dependence*,' but it is also true that conventional wisdom dictates that Category D drugs and/or Schedule II substances, i.e., barbiturates (and Secobarbital/Seconal being one,) in Pregnancy must be prescribed ***'to treat serious disease'*** in pregnant women, and for that matter, ***'oral prescriptions/orders'*** must be prescribed ***only*** and ***if*** needed in a *genuine emergency* and in a *limited quantity*, and not exploited as ***reckless 'parking' contraptions***, in the middle of the night, because the dreadful reality of ***'respiratory'*** and ***'vasomotor' depression!*** Therefore, I would like to respectfully recommend that when the FDA continues to maintain Category D with an unequivocal and strong proviso "*. . . if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective*," indirectly also compassionately covers other significant concerns such as the directive of Tile 21 USC Section 829--Prescriptions, i.e.,***'oral prescriptions/orders'*** must be prescribed ***only*** and ***if*** needed in a *genuine emergency* and in a *limited quantity*, **and** most importantly address the dreadful reality of ***'respiratory'*** and ***'vasomotor' depression*** issue.

All in all, I would like to thank you for giving me the opportunity to address my observations to you relating to FDA's Drugs Use-in-Pregnancy, Category D. This, in the sincere hope that you would seriously promote to maintain the unequivocal and strong proviso that barbiturates (and Secobarbital/Seconal being one,) be prescribed **only** and **if** ***to treat serious disease in pregnant women. . .*** which has already been gracefully adapted by the drug and medical reference *icons* in the Healthare Industry. As I look forward to hearing from you, I would like to express my *sincere* gratitude for your courtesies, time, and consideration. Indeed, ***"every unborn well-being is a sacred trust!"***

Respectfully Yours.

Rosario Zisa, C.P.A.

RZ/

cc: Jane E. Henney, MD, FDA's Commissioner
Bernard A. Schwetz, MD, FDA's Director of NCTR
Donna E. Shalala, Health and Human Service Secretary.